

MARK S. CHEE ET AL.  
Application No.: 08/327,525  
Page 2

PATENT

10 said computer system comparing said plurality of probe  
11 intensities; and  
12 identifying said unknown base according to results of  
13 said comparing step.

1 61. The method of claim 60, wherein said comparing  
2 step includes the step of said computer system calculating a  
3 ratio of a higher probe intensity to a lower probe intensity.

1 62. The method of claim 61, wherein said identifying  
2 step includes the step of identifying said unknown base<sup>plcya</sup> according  
3 to a nucleic acid probe having said higher probe intensity if  
4 said ratio is greater than a predetermined ratio value.

1 63. The method of claim 62, wherein said predetermined  
2 ratio value is approximately 1.2.

1 64. The method of claim 60, further comprising the  
2 step of sorting said plurality of probe intensities before said  
3 comparing step.

1 65. The method of claim 60, wherein said at least one  
2 sequence includes a reference sequence.

1 66. The method of claim 65, wherein said comparing  
2 step includes the step of said computer system comparing probe  
3 intensities of a probe hybridizing with said sample sequence to  
4 said probe hybridizing with said reference sequence.

1 67. The method of claim 65, wherein said comparing  
2 step includes the step of calculating first ratios of a wild-type  
3 probe intensity to each probe intensity of probes hybridizing  
4 with said reference sequence, wherein said wild-type probe  
5 intensity indicates an extent of hybridization of a complementary  
6 probe with said reference sequence.

MARK S. CHEE ET AL.  
Application No.: 08/327,525  
Page 3

PATENT

1 68. The method of claim 67, wherein said comparing  
2 step includes the step of calculating second ratios of the  
3 highest probe intensity of a probe hybridizing with said sample  
4 sequence to each probe intensity of probes hybridizing with said  
5 sample sequence.

1 69. The method of claim 68, wherein said comparing  
2 step includes the step of calculating third ratios of said first  
3 ratios to said second ratios.

1 70. The method of claim 69, wherein said identifying  
2 step includes the step of identifying said unknown base according  
3 to said probe associated with a highest third ratio.

1 71. The method of claim 68, wherein said comparing  
2 step includes the step of calculating a ratio of a highest probe  
3 intensity of a probe hybridizing with said reference sequence to  
4 a highest intensity of a probe hybridizing with said sample  
5 sequence.

1 72. The method of claim 71, wherein said comparing  
2 step includes the step of comparing said ratio to an *equivalent*  
3 ratio of neighboring nucleic acid probes.

1 73. The method of claim 65, wherein probe intensities  
2 of probes hybridizing with said reference sequence are from a  
3 plurality of experiments.

1 74. The method of claim 73, wherein said comparing  
2 step includes the step of said computer system comparing probe  
3 intensities of probes hybridizing with said sample sequence to  
4 statistics about said plurality of experiments.

1 75. The method of claim 74, wherein said statistics  
2 include a mean and standard deviation.

MARK S. CHEE ET AL.  
Application No.: 08/327,525  
Page 4

PATENT

1                   76. The method of claim 73, further comprising the  
2 step of normalizing said plurality of probe intensities by  
3 dividing each probe intensity by a sum of related probe  
4 intensities, wherein related probe intensities are from probes  
5 that differ by a single base.

1                   77. The method of claim 60, further comprising the  
2 step of subtracting a background intensity from each of said  
3 plurality of probe intensities.

1                   78. The method of claim 60, further comprising the  
2 step of setting a probe intensity equal to a positive number if  
3 said probe intensity is less than or equal to zero.

1                   79. The method of claim 60, further comprising the  
2 step of indicating said unknown base is unable to be identified  
3 if said plurality of probe intensities have insufficient  
4 intensity to identify said unknown base.

1                   80. The method of claim 60, wherein said unknown base  
2 is identified as being A, C, G, or T.

1                   81. In a computer system, a method of identifying an  
2 unknown base in a sample nucleic acid sequence, said method  
3 comprising the steps of:  
4                   inputting a plurality of probe intensities for a  
5 plurality of nucleic acid probes, each probe intensity indicating  
6 an extent of hybridization of a nucleic acid probe with said  
7 sample sequence, and each nucleic acid probe differing from each  
8 other by a single base;  
9                   said computer system calculating a ratio of a higher  
10 probe intensity to a lower probe intensity; and  
11                   identifying said unknown base according to a nucleic  
12 acid probe having said higher probe intensity if said ratio is  
13 greater than a predetermined ratio value.

MARK S. CHEE ET AL.  
Application No.: 08/327,525  
Page 5

PATENT

82. The method of claim 81, wherein said predetermined ratio value is approximately 1.2.

83. The method of claim 81, further comprising the step of sorting said plurality of probe intensities before said comparing step.

84. The method of claim 81, further comprising the step of subtracting a background intensity from each of said plurality of probe intensities.

85. The method of claim 81, further comprising the step of setting a probe intensity equal to a positive number if said probe intensity is less than or equal to zero.

86. The method of claim 81, further comprising the step of indicating said unknown base is unable to be identified if said plurality of probe intensities have insufficient intensity to identify said unknown base.

87. The method of claim 81, wherein said unknown base is identified as being A, C, G, or T.

88. In a computer system, a method of identifying an unknown base in a sample nucleic acid sequence, said method comprising the steps of:

inputting a first set of probe intensities, each probe intensity in said first set indicating an extent of hybridization of a nucleic acid probe with a reference nucleic acid sequence, and each nucleic acid probe differing from each other by a single base;

inputting a second set of probe intensities, each probe intensity in said second set indicating an extent of hybridization of a nucleic acid probe with said sample sequence, and each nucleic acid probe differing from each other by a single base;

MARK S. CHEE ET AL.  
Application No.: 08/327,525  
Page 6

PATENT

14 said computer system comparing at least one of said  
15 probe intensities in said first set and at least one of said  
16 probe intensities in said second set; and  
17 identifying said unknown base according to results of  
18 said comparing step.

1 ~~89~~ The method of claim 88, wherein said comparing  
2 step includes the step of calculating first ratios of a wild-type  
3 probe intensity to each probe intensity of probes hybridizing  
4 with said reference sequence, wherein said wild-type probe  
5 intensity indicates an extent of hybridization of a complementary  
6 probe with said reference sequence.

1 90. The method of claim 89, wherein said comparing  
2 step includes the step of calculating second ratios of the  
3 highest probe intensity of probes hybridizing with said sample  
4 sequence to each probe intensity of a probe hybridizing with said  
5 sample sequence.

1 91. The method of claim 90, wherein said comparing  
2 step further includes the step of calculating third ratios of  
3 said first ratios to said second ratios.

1 92. The method of claim 91, wherein said identifying  
2 step includes the step of identifying said unknown base according  
3 to said probe associated with a highest third ratio.

1 93. The method of claim 88, wherein said comparing  
2 step includes the step of calculating a ratio of a highest probe  
3 intensity in said first set to a highest intensity in said second  
4 set.

1 94. The method of claim 93, wherein said comparing  
2 step further includes the step of comparing said ratio to an  
3 analogous ratio of neighboring nucleic acid probes.

MARK S. CHEE ET AL.  
Application No.: 08/327,525  
Page 7

PATENT

95. The method of claim 88, further comprising the step of subtracting a background intensity from each of said plurality of probe intensities.

96. The method of claim 88, further comprising the step of setting a probe intensity equal to a positive number if said probe intensity is less than or equal to zero.

97. The method of claim 88, further comprising the step of indicating said unknown base is unable to be identified if said plurality of probe intensities have insufficient intensity to identify said unknown base.

98. The method of claim 88, wherein said unknown base is identified as being A, C, G, or T.

99. In a computer system, a method of identifying an unknown base in a sample nucleic acid sequence, said method comprising the steps of:  
inputting statistics about a plurality of experiments, each of said experiments producing probe intensities, each probe intensity indicating an extent of hybridization of a nucleic acid probe with a reference nucleic acid sequence, and each nucleic acid probe differing from each other by a single base;  
inputting a plurality of probe intensities, each probe intensity indicating an extent of hybridization of a nucleic acid probe with said sample sequence, and each nucleic acid probe differing from each other by a single base;  
said computer system comparing at least one of said plurality of probe intensities with said statistics; and  
identifying said unknown base according to results of said comparing step.

100. The method of claim 99, wherein said statistics include a mean and standard deviation.

MARK S. CHEE ET AL.  
Application No.: 08/327,525  
Page 8

PATENT

1 101. The method of claim 99, further comprising the  
2 step of normalizing said plurality of probe intensities by  
3 dividing each probe intensity by a sum of related probe  
4 intensities, wherein related probe intensities are from probes  
5 that differ by a single base.

1 102. The method of claim 99, further comprising the  
2 step of subtracting a background intensity from each of said  
3 plurality of probe intensities.

1 103. The method of claim 99, further comprising the  
2 step of setting a probe intensity equal to a positive number if  
3 said probe intensity is less than or equal to zero.

1 104. The method of claim 99, further comprising the  
2 step of indicating said unknown base is unable to be identified  
3 if said plurality of probe intensities have insufficient  
4 intensity to identify said unknown base.

1 105. The method of claim 99, wherein said unknown base  
2 is identified as being A, C, G, or T.--

REMARKS

Claims 60-105 are pending in the subject application. In a sincere effort to expedite prosecution Applicants canceled claims 1, 3-20 and 45-59. However, Applicants reserve all right to pursue these or other claims in another application. In light of the amendments and following remarks, Applicants believe all claims now pending are in condition for allowance.

Claims 1, 3-20 and 45-59 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject invention. Claims 1, 3-20 and 45-59 were rejected under 35 U.S.C. § 103 as being unpatentable over WO 92/10588 by Fodor et al. ("Fodor") in view of U.S. Patent No. 5,470,710, issued November 28, 1995 to Weiss et al. ("Weiss") and U.S. Patent No.